| HEALTH TECHNOLOGY APPRAISAL: NICE Health Technology Appraisals for Osteoporosis – Response to the DSU Report | |
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| **TO: NICE** | **FROM: NHS Quality Improvement Scotland** |

**Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women**

**and**

**Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women**

Reviewer 1

In terms of the base case used in this analysis, we would like to make the following specific comments:

- There is particular concern as to why an arbitrary £20,000 cut-off has been adopted for both primary and secondary prevention. This is a significant change from the previous ACDs and devalues osteoporosis as a disease compared with other conditions and puts less value on the suffering of our members compared with others.
- By including only those with "acute" fracture in the self-identification group, many women with a previous fragility fracture and at high risk of future fracture will be excluded from appropriate intervention. This is a significant step backwards from the existing NICE guidance on secondary prevention. Furthermore, most epidemiological data linking prior fracture to future fracture relates to fractures that occurred many years previously. The report suggests that it may be cost-effective to opportunistically assess women over 70 in a GP clinic, however there are concerns that in practice this will not happen, particularly as osteoporosis is not included in the Quality and Outcomes Framework of the General Medical Services contract.
- Noted that the fracture costs used in the base case are the same as those that have been used in previous analyses. These costs are now out of date and we would urge NICE to include the costs that were calculated by Stevenson et al (in press), which are more closely aligned to the findings of other studies in clinical practice, prior to issuing any ACD. Pleased to note that NICE has included home help costs in the sensitivity analysis and would like to see these included in the fracture costs for the base case.
- Noted that during the consultation period the price of alendronic acid on the Prescription Pricing Authority website has now decreased to £13.27 for 4 tablets.

We are concerned that from these analyses etidronate may be considered as the most cost effective treatment for some patients and hope that that when the new price for alendronic acid is incorporated it will result in alendronate/risedronate becoming the preferred treatment option.

- In the analysis for those women who present with a self-identifying risk factor (acute fracture, rheumatoid arthritis and high dose glucocorticoids) NICE should ensure that a list of medical conditions, other than rheumatoid arthritis, which are known to have a significant effect on fracture risk are also included as self-identifying risk factors.
- There is concern that the efficacy data for the bisphosphonates has reduced in each of the analyses that have been performed, with the decrease in this analysis being due to the pooling of the data for alendronate and risedronate. We would like to see the efficacy of alendronate being used throughout the analysis, even if this means that alendronate alone becomes the first line treatment.
- Concern remains that the "utility multiplier" values used for all fractures may be too high. In particular, the figure used for vertebral fractures does not reflect the true impact that multiple vertebral fractures have on a woman's quality of life. The model also still fails to incorporate morphometric fractures which, if progressive, are associated with significant morbidity for women in terms of, loss of height, kyphosis and functional impairment.

General concerns:

- As articulated in previous submissions to this process, it would be unacceptable if the committee were to deny preventative treatment to women under the age of 70 years in the opportunistic group. Although understanding the need to include cost effectiveness arguments when considering recommendations, we would urge NICE to ensure that osteoporosis is treated in the same way as other disease areas where prevention is key. This analysis could result in recommendations that would mean a woman younger than 70 years, who is at the same absolute risk of fracture as an older woman, would be denied treatment. This is at odds with current clinical practice.
- NICE should ensure that a range of alternative second line treatments are available to clinicians and patients when the ACDs are developed for all patients, regardless of age. In particular, although we continue to believe that the protective effect of raloxifene should not be an over-riding factor in determining how it is used in practice, it is to be hoped that when developing the ACD, NICE does ensure that raloxifene remains available as a treatment for those women in whom bisphosphonates or strontium ranelate are not tolerated or are contra-indicated. NICE are penalising the bisphosphonates heavily for their side effects and therefore it is not consistent to make no concession for beneficial effects.
- This analysis suggests that all patients will require a DXA scan prior to receiving treatment. Patients have voiced concern about being able to access DXA services immediately after a clinical vertebral fracture, where it is not necessary to indicate the likely effectiveness of treatment, or hip fracture where frailty may inhibit the option of carrying out DXA. Patients should not be denied therapy if no immediate DXA is available but rather should be able to start therapy while DXA is awaited. Furthermore, current DXA provision, while improving, is inadequate for the additional referrals that this guidance will create and will be

further stretched when the new WHO guidance is published. It is noted with disappointment that the costs for increasing provision have not been included in this analysis.

On publication, this new guidance will need to be explained to the patients etc who contact the NOS for information. Many of these people feel that the process of developing these TAs has been overly complicated and protracted. The results from the current analysis do not reflect the patient population in terms of those requiring preventative treatment in particular. NICE should produce guidance that does reflect the whole patient population and that can be fully understood and smoothly implemented by professionals and non-professionals alike.

Reviewer 2.

This complex exercise in mathematical modelling is just that - a mathematical exercise, whose relationship to reality is unknown. The outcomes are dependent upon the assumptions - and these have been well described.

I note that the three 'self-identifying' risk factors that are included in the model are 'an acute fracture', rheumatoid arthritis and high doses of glucocorticoids. There are no published data relating to raloxifene, strontium and teriparatide in the context of glucocorticoid associated osteoporosis. Are other risk factors permissible ? It should be noted that some of the analyses include the requirement for 3 self-identifying risk factors - the concurrence of fracture + high dose steroids + rheumatoid disease would be rare and frankly of little practical relevance to the public health problem of prevention of osteoporotic fractures.

If I understand the scenario base-case 1 on p17 - and Table 13 p39 whether by opportunistic assessment or 'self-identifying' risk factors, DXA should not be offered to women under 70, with history of a fracture, presumably because there isn't a BMD at which treatment with alendronate or risedronate is cost effective. The NICE technology appraisal suggested that patients over 70-75yr with fracture might be treated, for fracture secondary prevention, without necessarily undergoing prior DXA. These two approaches do not appear to be compatible.

It is also not plausible that there is not a BMD threshold that a patient with a fracture might have at the age of 65yr that might merit treatment for fracture secondary prevention. It should also be remembered that a fracture patient today at age 65yr, is at twice the fracture risk of somebody age 65yr without fracture; in 5years' time this patient will be aged 70yr and then be eligible for assessment for treatment. To preside over the natural history of osteoporosis and fractures under the age of 70yr may be the recommended outcome of this mathematical modelling exercise - but as a clinician I recognise the opportunities that exist to reduce the burden of osteoporotic fractures and I recognise what is reasonable expectation for intervention among these patients and this document appears to neglect both.

Our own service model (based on deployment of Osteoporosis Nurse Specialists working in a Fracture Liaison Service) links acute fracture presentations to A&E and orthopaedics with automatic post-fracture osteoporosis assessment - and doesn't necessitate opportunistic discussions about fractures or awareness of self-identifying risk factors within a primary care setting. It would be interesting to model the theoretical

impact of this approach that cuts out the need for case-finding in primary care. Our reference is: McLellan et al. OI 2003; 14: 1028-1034.

There are no data relating to non-vertebral fracture efficacy with treatment with etidronate and no data relating to efficacy of teriparatide in reducing hip fractures - so modelling their impact on fracture outcomes must reflect this.

As regards Appendix 2: I have no comment on this, other than to recommend that the authors, if they haven't done so, should contact Dr Opinder Sahota who has recently recosted hip fractures (in Nottingham).

28 August 2006